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THE REGULATION OF RAT ACTIVITY FOLLOWING EXPOSURE TO HYPERDYNAMIC FIELDS

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INTRODUCTION

The microgravity of spaceflight and the hyperdynamic fields produced via centrifugation have allowed researchers to examine the effect of altered gravitational environments on the regulation of physiological systems. In previous studies (2,5), we have discussed the importance of homeostatic and circadian mechanisms for the regulation of physiological systems such as body temperature and heart rate. Rats exposed to a chronic 2G field exhibited lower mean daily body temperature and heart rate. The homeostatic component of regulation for body temperature and heart rate adapts to a new steady state after 5-6 days. However, the circadian rhythm of body temperature and heart rate became severely depressed and did not recover for approximately 7-10 days (1,2,5).

The measurements of body temperature and heart rate suggest an adaptation of homeostatic and circadian regulatory mechanisms following 10 days exposure to 2G. However, an important function of physiological homeostasis is to respond to environmental stressors. An important question thus becomes whether the regulation of body temperature and heart rate has sufficiently recovered to respond to an environmental challenge separate from that of the hyperdynamic field.

In this study, a high frequency light/dark cycle (LD 3:3) was provided for 24 hours as an environmental challenge to assess the recovery of homeostatic and circadian regulation. Previous studies (3,5) have demonstrated that high frequency light dark cycles are highly effective for testing homeostatic and circadian components of physiological regulation in monkeys (3) and rats (5). For example, the nocturnal rat exhibited a homeostatic increase in body temperature during the dark periods and a decrease during the light periods. In addition, the magnitude of the body temperature response exhibits a time of day variation demonstrating the effect on circadian regulation.

MATERIALS AND METHODS

Eight male albino Wistar rats were anesthetized and surgically implanted with a biotelemetry unit (Mini-Mitter) in the peritoneal cavity. Following recovery, the animals were singly housed in cages on of an 18 ft diameter centrifuge. A receiver board located under each rat cage is interfaced with a computer to monitor the animal's activity every 10 minutes. Animals were exposed to 12 hours of lights and 12 hours of dark (LD 12:12) with *ad libitum* food and water. After a one week 1G control period the animals were exposed to a high frequency light/dark cycles alternating between 3 hours of light and 3 hours of dark (LD 3:3) for a period of 24 hours. One week following the first LD 3:3, the animals were exposed to 2G field for 6 weeks. Two days after the onset of 2G the animals were exposed to the second period of LD 3:3 followed by LD 3:3 exposure at weekly intervals. Measurements of mean daily activity, circadian amplitude, and the relative differences in activity between light and dark periods of LD 3:3 were compared across conditions using analysis of variance.

RESULTS

Homeostatic Changes. Figure 1A illustrates the change in mean daily activity for all the rats following exposure to 2G. There was a rapid 80% decrease in mean daily activity between the last day of control and the first day of 2G, followed by gradual increase in activity until adaptation to a new steady state was reached by day seven. However, mean daily activity at this adaptation level remained 29% below that of baseline. The control, initial response to 2G, and adapted periods were statistically compared by examining the averaged mean daily activity over seven days. There was a significant difference between the daily mean activity of control,, the initial response to 2G and adaptation ($F = 35.8$, $df = 2, 18$, $p < 0.001$). A Tukey's test also demonstrated that mean daily activity exhibited a statistically significant decrease between the 1G control and the initial response to 2G. In addition, there was a statistically significant increase in mean daily activity between the initial response and adaptation, but the adapted level remained significantly below that of baseline.

Circadian Changes. Figure 1B illustrates the change in the circadian amplitude of activity during 1G, initial 2G response, and 2G adaptation. Circadian amplitude exhibited an 80% decrease between the last day of baseline and the first day of 2G. There was a gradual recovery of circadian amplitude, but the adaptation occurred by the ninth day which was later than that for mean daily activity. The circadian amplitude during the first day of adaptation remained 45% below baseline. The control, initial 2G response and 2G adaptation was compared as described previously. The change in circadian rhythm amplitude of activity between the control and initial response, and adaptation to 2G was significant ($F = 61$, $df = 2, 18$, $p < 0.001$). A Tukey's test demonstrated that the decrease in circadian amplitude of activity between 1G and the initial 2G response of was statistically significant. In addition, there was a statistically significant increase in activity amplitude from the initial response and the period of adaptation. However, the amplitude during adaptation remained significantly below that of the baseline control.

LD 3:3 Responses. Figure 2 illustrates the effect of high frequency light/dark cycles by comparing the pattern of activity during a 24 hour period of LD 3:3 at 1G and LD 3:3 periods during 2G. During LD 3:3, the 3 hour light periods during the subjective night suppressed activity, while the 3 hour dark periods during the subjective day increased activity. Therefore there was greater activity during the four 3 hour dark periods than the four 3 hour light periods. The second exposure to LD 3:3 occurred during the second day of 2G. There was no difference in

overall activity between the 4 dark periods and 4 light periods which was a decrease of 102% relative to 1G. On the third exposure to LD 3:3 (ninth day of 2G) there was an increase in overall activity and a slight circadian rhythm. However, there was still no response to LD 3:3 (a decrease of 88%). By the fourth exposure to LD 3:3, there was a distinct circadian rhythm and response to LD 3:3, but the response was still below 51% that of the 1G.

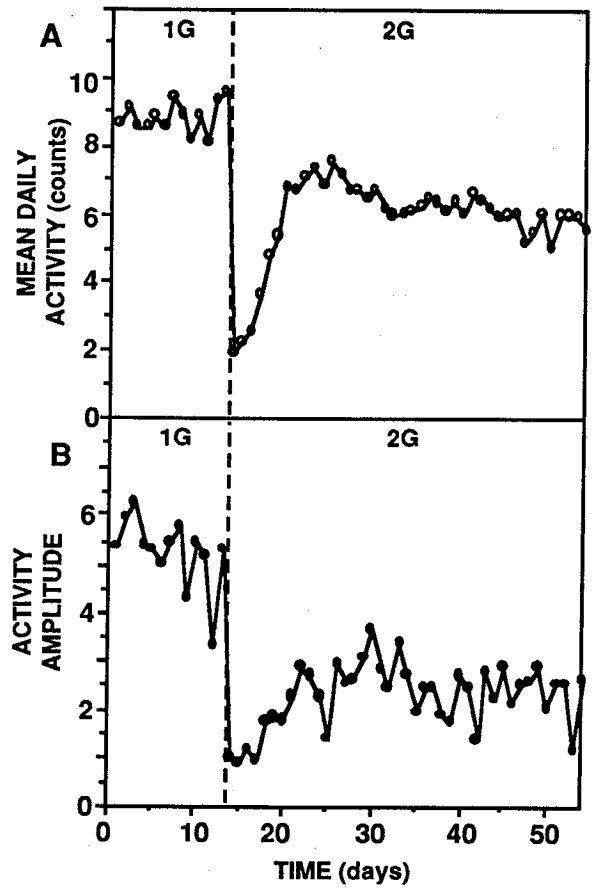

FIGURE 1. THE EFFECT OF 2G ON MEAN DAILY ACTIVITY AND CIRCADIAN RHYTHM AMPLITUDE.

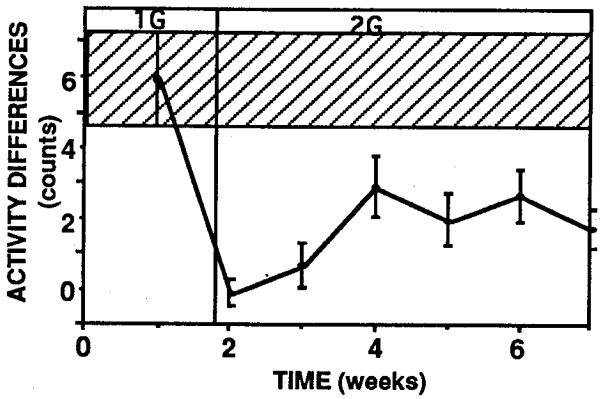

FIGURE 2. DIFFERENCES IN ACTIVITY BETWEEN DARK AND LIGHT PERIODS.

DISCUSSION

The results of this study demonstrate that exposure to 2G via centrifugation has significant effects on the regulation of activity. The components of homeostasis and circadian rhythms that regulate activity are both affected by 2G. The homeostatic component exhibited a significant decrease in mean daily activity in response to 2G, which adapted to a new steady state that was significantly less than the 1G control. The circadian component exhibited a significant decrease in circadian rhythm amplitude following exposure to 2G, which adapted to a new steady state significantly below the baseline 1G. In addition, mean daily activity adapted to a new steady state before that of the circadian rhythm amplitude. The effects of 2G on activity regulation was similar to that of body temperature reported previously (4,5). Body temperature exhibited a significant decrease in mean daily body temperature and circadian rhythm amplitude, and the adaptation of mean daily body temperature occurred before that of circadian amplitude. However, one difference between the physiological parameters is that the suppression of body temperature rhythm amplitude was gradual over the course of several days, but the circadian rhythm amplitude of activity exhibited an immediate decrease.

This study also demonstrated that high frequency light/dark cycles significantly alter the pattern of activity. When the animals are exposed to chronic 2G, there is change in the homeostatic and circadian regulation of activity. During this time, the animal's activity fails to respond to the high frequency light/dark cycles. Following the adaptation of mean activity and circadian amplitude, the pattern of activity becomes responsive to high frequency light/dark cycles. It appears that the recovery of mean daily activity and the circadian rhythm of activity are necessary in order to functionally respond to high frequency light/dark cycles. However, our previous study on body temperature (5) demonstrated important differences from that of activity. Body temperature was responsive to the effects of high frequency light/dark cycles (LD 3:3) immediately following 2G exposure when there is a decrease in mean daily body temperature, but not a complete suppression of circadian rhythm amplitude. This suggests that the circadian component is critical for the physiological response to high frequency light/dark cycles. Future studies will determine the relative role of homeostatic and circadian components in the regulation of physiological systems and adaptation to changes in gravity.

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